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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/296,534	04/22/99	HALLOWITZ R	BIOTI-7

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EXAMINER	
ZEMAN,R	
ART UNIT	**PAPER NUMBER**
1645	5

DATE MAILED: 02/25/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/296,534	Hallowitz et al.
Examiner	**Group Art Unit**
Robert A. Zeman	1645

☒ Responsive to communication(s) filed on *Apr 22, 1999* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-17* is/are pending in the application.

Of the above, claim(s) *17* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-16* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Priority

This application is a continuation-in-part application of 09/139,663, filed on 8/25/98 which is a 371 National Stage of PCT/US97/18649, filed 10/15/97, which is a continuation-in-part application of 08/732,782 filed on 10/15/96, now U.S. Patent No. 5,817,458 and application 08/732,784 filed 10/15/96, now U.S. Patent No. 5,714,390. Applicant has referred to application 09/139,663 as 09/139/633 throughout the specification. Proper corrections are required.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

It does not state that the person making the oath or declaration in a continuation-in-part application filed under the conditions specified in 35 U.S.C. 120 which discloses and claims subject matter in addition to that disclosed in the prior copending application, acknowledges the duty to disclose to the Office all information known to the person to be material to patentability as defined in 37 CFR 1.56 which occurred between the filing date of the prior application and the national or PCT international filing date of the continuation-in-part application.

withdrawn in light of amendment - present tense to examples not performed.

Specification

The specification is objected to because Applicant uses more than one grammatical tense (see Example 2, page 16) and switches between them frequently making it unclear whether procedures have actually been performed. Correction is required. See MPEP § 608.01(b).

Claim Objections

withdrawn

Claims 2, 6-8 and 10 are objected to because of the following informalities: The use of the plural "claims" when referring to a single claim. For example "A method of **claims 1**...." Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the OM-10.1, U1, and Jurkat cell lines are required in order to practice the claimed invention. Specifically, it is noted that claim 16 recites deposited material in the body of the claim. Applicant must either demonstrate these cell lines are either well known and readily available to the public or must deposit the material in accordance with 37 CFR 1.808. The

deposit of biological organisms is considered by the Examiner to be necessary for enablement of the current invention {see 37 CFR 1.808(a)}.

If a deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, than an affidavit or declaration by Applicants or person(s) associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, should be submitted stating that the deposit has been made at an acceptable depository *and that* the following criteria have been met:

1) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

2) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

3) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

4) a viability statement in accordance with the provisions of 37 CFR 1.807; and

5) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 14 are rendered vague and indefinite through the use of the term "capable of". Simply having the capacity to do something does not mean that it is actually done. Consequently, it is impossible to determine the metes and bounds of the claimed invention.

Claim 1 is rendered vague and indefinite by the use of the term "treating". It is unclear what Applicant is claiming hence it is impossible to determine the metes and bounds of the claimed invention.

Claims 2, 9 and 10 are deemed to be vague and indefinite. It is impossible to determine when and how the recited method steps are to be performed. Are the cells obtained before or after treatment? How is CD4 and CD8 separation to be accomplished? Through the use of anti-gp120? To which fraction? As written, it is impossible to determine the metes and bounds of the claimed invention.

Claim 2 is rendered vague and indefinite by the use of the term "obtaining sample cell population". It is unclear what Applicant is claiming. What type of sample? From where is it obtained? Is it a primary cell population? From an established cell culture? A single time point? As written it is impossible to determine the metes and bounds of the claimed invention.

Claim 3 is vague and indefinite due to the use of the phrase "each conjugated to a capture moiety" It is unclear whether "each" is referring to the cells or antibodies. Which is conjugated to the capture moiety? Additionally, the use of the terms "labeled-cells" and "complex-labeled cells" is confusing. What is the difference between the two? As written it seems that Applicant is contacting the samples cells with the capture moiety in successive steps. To what end? Addition of the same substance will not change the composition.

Claims 3-5 is vague and indefinite since it is unclear what is meant by "capture moiety"?. Does it interact directly with the cell? Or is merely a label? If its a label, why infer that it actively "captures" something? Consequently, for the aforementioned reasons it is impossible to determine the metes and bounds of the claimed invention.

Claim 7 is rejected as it does not further limit its antecedent claim. Claim 5 recites "a magnetic bead" whereas claim 7 recites "magnetic particles". It is unclear whether the two are in fact the same entity with the same physical and biological properties. If they are the same, it is preferable to use consistent terminology throughout the claims.

Claim 8 is rejected as vague and indefinite due to the phrase "the removing". The removing of what? It is unclear what Applicant is claiming and impossible to determine the metes and bounds of the claimed invention.

Claim 12 is rejected as vague and indefinite since it recites a the limitation "tissue is lymphoid". There is no antecedence for this limitation in claim 1 on which claim 12 is dependent.

Claim 14 is rejected as vague and indefinite. It is unclear what Applicant means by "treating the resting with....". What is "resting" referring to? As written it is impossible to determine the metes and bounds of the claimed invention. It is believed that one or more words have been omitted. For the purposes of this examination the term "resting" will be interpreted as "resting lymphoid cells".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Applicant has claimed the priority date of 10/15/1996 based on the parent case 09/139,663 (not 09/139,633) of which it is a continuation-in-part and which is a continuation of PCT/US97/18649. It has been deemed that all references to "methods of determining latent viral load" and the use of the reagents for that purpose constitutes matter not disclosed or enabled in the parent case and, as such, is not entitled to said priority date. Consequently, the priority date used with regards to the aforementioned matter is 4/22/99.

Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chun et al (Nature Vol. 387, pages 183-188 May 1997) in view of Chun et al.(Nature Medicine Vol. 1 Number 12, pages 1284-1290. December 1995) and Essex et al. (U.S. Patent 4,725,669).

The aforementioned claims are drawn to methods of determining latent viral load in a host infected with HIV through: the selection of "resting lymphoid cells" through the utilization of magnetic beads and antibodies to various cell markers including, CD4, CD8, HLA-DR and gp120; subsequent stimulation of said cells with a phorbol ester or cytokine to induce latent virus; and using the presence of gp120 on cell surfaces as a indicator of latent infection. Chun et al (Nature Vol. 387, pages 183-188 May 1997) disclose methods for the "quantification of latent tissue reservoirs" that entails the isolation of resting $CD4^+$, HLA-DR^- cells from lymph nodes and blood (see page 183, 2nd paragraph). The resting $CD4^+$, HLA-DR^- cells (resting lymphoid cells) were obtained through sequential magnetic bead depletion (CD8 and HLA-DR, as well as other antibodies, were coupled to magnetic beads) and positive selection using CD4 labeled beads (see figure 1 legend and page 1289 column 2 of Chun et al. Nature Medicine Vol. 1 Number 12, pages 1284-1290. December 1995, which is cited as methods used in Chun et al Nature Vol. 387, pages 183-188 May 1997). The resting lymphoid cells were then treated with the phorbol ester phytohaemagglutinin (PHA) to stimulate activation of the latent HIV. Virus production was measured by p24 ELISA. Chun et al. differs from the recited claims in that they do not use anti-gp120 coupled to magnetic beads for the depletion of cells actively infected with HIV or do they use the appearance of gp120 on the "stimulated" resting cells as the indicator of latent virus production. Additionally, Chun et al. do not use cytokines to stimulate latent virus production in the "resting cells". Essex et al. (U.S. Patent 4,725,669), however, disclose that "a protein having a molecular weight of approximately 120,000 daltons (gp120) occurs on the cell surface of cells infected with HTLV-III (HIV-1) and determines whether or not an

immunocomplex is formed" (see column 2 lines 13-22). Moreover, Essex et al. disclose that the presence of gp120 in a biological specimen is indicative of cells actively infected by the HTLV-III (HIV-1) virus and that an assay for gp120 is a useful diagnostic procedure for determining such infection in biological specimens (see abstract). Consequently it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the gp120 marker and gp120 disclosed by Essex et al. in the methods for obtaining "resting lymphoid cells" disclosed by Chun et al. One having ordinary skill in the art would have been motivated to do this since the presence of gp120 on a cell surface is indicative of lymphoid cell activation, it would allow one to streamline the purification process (i.e. reduce the they number of cell markers needed to purify the lymphoid sample) and the detection process thereby reducing time and other resources needed .

Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chun et al (Nature Vol. 387, pages 183-188 May 1997) in view of Chun et al. (Nature Medicine Vol. 1 Number 12, pages 1284-1290. December 1995) and Essex et al. (U.S. Patent 4,725,669) and Chun et al (Journal of Experimental Medicine. Vol. 188 Number 1, July 6, 1998 pp 83-91).

Claim 13 is drawn to the treating of isolated "resting lymphoid cells" by either a phorbol ester or a cytokine to activate latent HIV. As detailed above, Chun et al. (Nature Vol. 387, pages 183-188 May 1997) disclose use of PHA for said activation. Chun et al. do not disclose the use cytokines (TNF-alpha, IL-1 and IL-6) for latent virus activation. However, Chun et al (Journal of Experimental Medicine. Vol. 188 Number 1, July 6, 1998 pp 83-91) disclose the use of several cytokines for the activation of HIV-1 replication in latently infected resting lymphoid

cells. Consequently it would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the phorbol ester activator disclosed by Chun et al. with the methods disclosed by Chun et al. and Essex et al. since IL-1, IL-6 ,TNF-alpha and phorbol esters all stimulate "resting" lymphoid cells to become "active".

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can be reached between the hours of 7:30 am and 4:00 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, Donna Wortman, Primary Examiner can be reached at (703) 308-1032 or the examiner's supervisor, Anthony Caputa, can be reached at (703)308-3995.

DONNA WORTMAN
PRIMARY EXAMINER

Robert A. Zeman

February 17, 2000